

Limited English Proficiency and Disparities in Clinical Research

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Introduction

Imagine that you possess an indicator for a disease or illness that has nothing to do with your body. It is not a genetic predisposition to acquire cancer or a vice that raises the probability of contracting some dread disease, though estimates of its health risks have placed it on par with having diabetes. It has nothing to do with the environmental pollutants you are exposed to or whether you can afford health care. It is not a physical susceptibility that renders you more easily reachable by the clutches of pathology. No, this indicator of health hinges on certain learned abilities and skills, and it is a barrier to health that is totally within the health field's power and resources to lift.

The condition hinted at above is the inability to speak English proficiently in the United States. Today, more than one-sixth of the United States' population speaks a language other than English *at home*¹ and this number (approximately 50 million people) is increasing rapidly.² Between 1990 and 2000, for example, the number of Americans who speak a language other than English at home increased by 15.1 million or 47 percent while those with limited English proficiency (LEP) rose by 7.3 million or 53 percent.³ According to the 2000 U.S. Census, over 8 percent of the total U.S. population either speaks no English, or does so "less than very well."⁴ The size of these populations and their percentage of the total population can both be expected to continue to increase for the foreseeable future.⁵ The Hispanic/Latino/a population alone has exhibited a 57.9 percent increase between 1990 to 2000 that has far outpaced the overall 13.2 percent increase for the populace as a whole.⁶ Additionally, 20 percent of patients report language barriers when attempting to communicate with health care providers.⁷ It is of critical importance that this growing segment of the population be able to communicate effectively with its health care providers in order to ensure safe and effective delivery of health care. It is also apparent that a continued failure to provide for linguistically appropriate health services only deepens the health disparities in this country. Effective communication is necessary for there to be any chance of the kind of information exchange required of the informed consent process, or for the understanding of and adherence to treatment regimens. The profound

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disability that LEP can be to patients is evident in the cases where there have been unnecessary errors that were directly attributable to the miscommunication between physicians and patients who did not share a common language.⁸

LEP in Clinical Research

While there exists research showing how limited English proficiency (LEP) negatively affects a patient's access to health services and quality of the care she receives,⁹ there are relatively few data on how LEP affects clinical research participants. The data that do exist point clearly to the fact that many clinical trials are often conducted with serious ethical, legal, and scientific shortcomings regarding the study population's LEP participants.¹⁰ Also, while there exist several studies of the medical errors committed due to the myriad ways in which doctors and LEP patients mistranslate and misunderstand each other in clinical contexts,¹¹ a literature review revealed none that dealt with errors attributable to LEP in clinical research contexts. However, I see no reason why there would not be similar incidence and severity of adverse events in clinical trials where LEP participants are enrolled.¹²

Limited English proficiency also renders potential participants vulnerable to coercion or undue influence in especially troubling ways. For instance, there is a real danger that LEP populations will be recruited into clinical research that they would otherwise not consent to. In such cases, it is not difficult to imagine an instance when an LEP patient, perhaps ashamed of her linguistic incapacity, attempts to compensate by being unduly deferential to and unquestioning of the physician-researcher and acquiesces despite having little understanding.¹³ These are troubling possibilities, especially given the fact that LEP participants are less likely to comprehend the information recited during the typically brief informed consent process that has become the norm in U.S. clinical trials.¹⁴ Nonetheless, this paper focuses on the exclusion from research since there is adequate evidence to suggest that LEP is more likely to result in the exclusion of this vulnerable population from clinical research than on improper inclusion.¹⁵

This article shows the barriers to adequate clinical trial access by LEP participants and explains why this is a legal, ethical, and scientific problem worthy of our attention. I demonstrate that laws, regulations, and guidelines already exist to protect from this type of discrimination, but that these are largely overlooked, under-utilized, and under-enforced. The paper con-

cludes with recommendations for clinical research institutions in light of the scientific, legal, and ethical imperatives identified here as well as a call for a reconsideration of the problem of the exclusion and inclusion of LEP participants in clinical trials.

The Scientific Imperative

Approximately 80,000 clinical trials are conducted in the United States each year¹⁶ and of those that participate in these trials, 88% are white¹⁷ (though they comprise roughly three-fourths of the U.S. population.)¹⁸ This relative lack of diversity in clinical trials is a troubling confounder to the scientific and statistical validity of research that relies on the principle of randomization to validly extrapolate and generalize findings to a general populace.¹⁹ If the subject population

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is relatively homogenous, then the research has the potential of delivering spurious findings when generalized to a more heterogeneous population. However, it is far from obvious that excluding those who have LEP has any potential to render the research findings scientifically spurious in this way. After all, no one is claiming that LEP status is a causal factor in differential pharmacokinetic response, for example. Nonetheless, I believe that there exist logical bases for at least a *prima facie* presumption that studies that exclude LEP participants and are thus, to a large extent, ethnically non-diverse yield results whose generalizability is compromised.²⁰

Although about 99.9 percent of genes across the human species are identical, the remaining 0.1 percent is important for a multitude of allelic attributes including the pharmacokinetic responses that individuals have toward drugs.²¹ Even now, relatively early in the post-genomic era, fully one-third of the over 10 million single-nucleotide polymorphisms (SNPs) that have been identified have been collected in the International HapMap Project database.²² These slight variations in the genomes of individuals are largely responsible for the sometimes wildly varying responses people have to pharmacologies, and they can greatly affect dis-

ease risk. Since these variations are inherited in blocks, a person's ancestral groups can be discovered because of signature SNPs found in the person's genome.²³ And since ancestral groups are commonly shared among a self-described ethnic group, the often culturally, geographically, and socially constructed term "ethnicity" begins to have salience as a pharmacogenomic indicator — albeit an imperfect one.

A thorough knowledge of the relative allele frequencies and patterns in ancestral groups will protect against unwanted reactions and ensure efficacy of new pharmacological agents for consumers. This pharmacogenomic and pharmacogenetic "tailoring" of drugs is thought to be the next revolution on the path to "personalized medicine."²⁴ Since LEP can often be an indicator of minority ethnicity (as Title VI and its subsequent guidance suggest by declaring discrimination against people of LEP as national origin discrimination), then the current exclusionary and discriminatory environment in which clinical trials are conducted is contributing to the non-generalizability of research findings. This is because "ethnicity," though a term with tenuous genomic relevance, remains a relatively good indicator for common ancestral groups.²⁵ These ancestral groups, in turn, often show distinct patterns of genetic allele frequency that are largely responsible for pharmacokinetic responses in patients.²⁶ These gene clusters constitute what in generalizability theory are known as "facets" or (possible) sources of variation in results.²⁷ Thus, excluding groups whose pharmacogenomic profiles may differ in relevant ways from other groups renders the study findings not universally generalizable until the underrepresentation of these facets is proven (through empirical research) to be inconsequential.²⁸ The vigilant inclusion of LEP participants, because of the fact that they may be likely to correspond to genetic ancestral groups that are currently underrepresented in clinical trials,²⁹ is by this logic a scientific necessity.³⁰

The Legal Imperative

In addition to the at least *prima facie* scientific necessity to include LEP participants in clinical trials,³¹ there exist further bases that brook no ambiguity in their defense.

Title VI of the Civil Rights Act of 1964

In the social tumult of the 1960s, the landmark law known as the Civil Rights Act effectively changed many of the institutional mechanisms that previously allowed *de facto* discrimination through disparate impact upon minorities. One of the more famous provisions of this law, Title VI, prohibits, *inter alia*, the denial of meaningful access for minority groups

to the services provided by any entity that receives federal funding.³² Among the services covered by the law, "clinical research programs" were specifically included.³³

Unlike most other codes, guidelines and laws dealing with the ethics of human subjects research, which have been promulgated as responses to ethically deplorable cases (such as the Nuremberg Code and the Belmont Report as responses to Nazi experimentation and the syphilis study at Tuskegee, respectively), the guidelines and laws dealing with minority access to clinical research stem more directly from a larger societal shift in thinking about issues of gender, ethnicity, and race that occurred in 1960s America of which the Civil Rights Act was one notable manifestation. The Civil Rights Movement and the Women's Liberation Movement both spawned vigorous debate nationally about issues of equality and justice and brought an awareness of many minority groups' historically unfair participation in clinical research. In the 19th and the first half of the 20th Century, immigrants were among the groups that bore more than their fair share of the burden of medical research.³⁴ Then, after scandals such as the one that erupted in the United States of America when the Tuskegee Syphilis Study was brought to the public's attention, minority groups became generally *underrepresented* in clinical trial populations.³⁵

NIH Revitalization Act

These scandals, along with the catalytic social upheaval of the 1960s resulted in various laws and policies to address the underrepresentation of certain groups in clinical trials. Among these, perhaps the one most directly aimed at the problem is the 1993 National Institutes of Health (NIH) Revitalization Act.³⁶ Among its many provisions, the NIH Revitalization Act significantly strengthened the NIH policies regarding the inclusion of minorities in research participation. Enacted in March 1994, the law states the following:

It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification establishes...that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research.³⁷

Executive Order 13,166

In 2000, President Clinton issued an Executive Order mandating that all federal agencies adopt guidelines for the removal of language barriers for persons with

LEP.³⁸ President Clinton's Executive order 13,166 "Improving Access to Services for Persons with Limited English Proficiency" required every federal agency that provided funds to non-federal entities to publish guidance on meaningful access for LEP persons and Title VI compliance.³⁹ The President ordered that "each Federal agency shall...develop and implement a system by which LEP persons can meaningfully access those services consistent with, and without unduly burdening, the fundamental mission of the agency."⁴⁰ The Executive Order goes on to mandate that "[e]ach Federal agency shall also work to ensure that recipients of Federal financial assistance provide meaningful access to their LEP applicants and beneficiaries."⁴¹

LEP Guidance

In accordance with this executive order, the U.S. Department of Health and Human Services (DHHS) Office of Civil Rights (OCR) announced guidelines in 2003 delineating the obligations that virtually all recipients of federal funding have to persons with limited English proficiency.⁴² The OCR based its interpretation on the sweeping obligations found in Title VI which state that no person shall "on the grounds of race, color, or national origin, be excluded from participation in, be denied benefits of, or be subjected to discrimination under any program or activity receiving Federal financial assistance."⁴³ This affirmative obligation that proscribed both intentional acts of discrimination and *de facto* ones was broadly interpreted and applied to all variety of health care contexts⁴⁴ including clinical research.⁴⁵ In these governmental decrees, LEP persons are defined as "[i]ndividuals who do not speak English as their primary language and who have a limited ability to read, write, speak, or understand English."⁴⁶

The guidance also clarifies that any institution that violates the Civil Rights statute may lose federal funding for "restrict[ing] an individual in any way in the enjoyment of any advantage or privilege enjoyed by others receiving any service, financial aid, or other benefit under the program" or for "utiliz[ing] criteria or methods of administration which have the effect of subjecting individuals to discrimination because of their race, color, or national origin, or have the effect of defeating or substantially impairing accomplishment of the objectives of the program as respects individuals of a particular race, color, or national origin."⁴⁷ The U.S. Supreme Court in *Lau v. Nichols* interpreted Title VI as forbidding *de facto* discrimination based on LEP status under the rubric of "national origin,"⁴⁸ though later, in *Alexander v. Sandoval*, the Supreme Court called into question the validity of the *de facto* discrimination standard when it made it far more

difficult for individuals to bring suit against entities under Title VI.⁴⁹

However, the OCR, the governmental office tasked with oversight on the issue of discrimination against LEP patients and participants, is underfunded and overburdened.⁵⁰ Ever since the *Sandoval* case, the OCR is policing this issue through administrative action on its own instead of allowing private actions to deflect some of the "legwork" of enforcement. The OCR has also suffered an enormous funding decrease (in adjusted 2007 dollars) from \$106 million in 1970 when it was established, to \$35 million in 2007, the last year for which an OCR budget was available as of this writing.⁵¹ Both of these facts (the lack of enforcement through private claims, and a shrinking OCR budget) reveal a governmental office whose responsibility has outgrown its financial resources. This state of affairs, along with an overall lax enforcement atmosphere by other governmental agencies as to minority inclusion into clinical trials, conspire to give us the present environment where laws and guidelines have been promulgated yet the problems they were aimed at solving remain.⁵²

Institutional Policies

According to Title VI and the OCR's 2003 guidelines, institutions that receive any federal funding must implement and maintain policies that ensure meaningful access to clinical trials for LEP participants (if inclusion would be appropriate, and if English proficiency is not necessary for the study to be scientifically valid.)⁵³ According to the 2003 guidance, in order to provide covered entities an alternative to an individualized compliance inquiry which is taxing on the already overburdened OCR, the LEP guidance introduces a Key Elements Safe Harbor provision. This offers health services providers assurance of Title VI compliance if they "effectively incorporate and implement" four elements: a comprehensive community needs assessment, a written policy on language access, personnel training, and vigilant monitoring.⁵⁴

LEP Key Elements Safe Harbor

To ease both the oversight burden on the DHHS's OCR, and to help assuage the fears that institutions may have of whether they are adequately complying with Title VI's rules, the OCR developed an "LEP Key Elements Safe Harbor" provision. Safe harbors are provisions in statutes or regulations that reduce or, in some cases, eliminate a party's potential liability under the law if the party complies with certain stipulations such as reporting requirements or evidencing the advancement towards full compliance. Safe harbor provisions usually protect those who are making

good faith efforts to comply with a demanding law or one that has the potential for varying interpretations.

Institutions that want the protection of the safe harbor are first required to undertake a comprehensive assessment of the language needs of the communities the institution serves. If the needs assessment shows that meaningful access to the institution's services is currently inadequate, then a written response plan should be sent to the OCR.⁵⁵ The needs assessment must use a four-factor analysis to make a determination of the adequacy of current language services in clinical trials. The OCR claims that this is to be a "flexible and fact-dependent standard"⁵⁶ wherein an individualized assessment of the following four factors is warranted:

- (1) the number or proportion of LEP persons eligible to be served or likely to be encountered by the program or grantee; (2) the frequency with which LEP individuals come in contact with the program; (3) the nature and importance of the program, activity, or service provided by the program to people's lives; and (4) the resources available to the grantee/recipient and costs.⁵⁷

For factors one and two of this analysis, it is important to note that the OCR is sensitive to the possibility that the needs assessment may in one very important sense be unfit to uncover the true language needs of the institution's participant demographic. That is, existing language barriers may explain why a population has historically been underrepresented in an institution's clinical research program. This kind of finding may in turn signal the necessity for outreach programs to that segment of the community.⁵⁸ The institution should therefore assess the frequency with which the target populations *should* have contact with the institution's clinical research program.⁵⁹ Whenever data other than historical records of the institution support this judgment, the analysis should compensate accordingly. The "other data" that might alert the institution to underserved populations might be, for example, local census figures and school system demographics.⁶⁰ There is, however, no absolute preset LEP demographic percentage that will automatically trigger the necessity to provide linguistically appropriate care.⁶¹ According to the 2003 OCR guidance, what is sufficient to trigger the necessity for affirmative LEP assistance will always be a context-dependent, case-by-case determination of what is "both necessary and reasonable in light of the four-factor analysis."⁶² Local surveys should also be updated at least biennially due to rapidly fluctuating demographics.⁶³

When assessing the nature and importance of the recipient's clinical research program for purposes of factor three in the needs assessment, the OCR guidance speaks of looking at both the importance and the urgency of the program to LEP individuals. If, for example, the clinical research program at the recipient institution is considered to be an important part of the institution's mission and service, then the more likely it is that it will be considered "important" for purposes of the third factor.⁶⁴ If the research is one of relative importance to medical knowledge and can be considered ultimately to be of possible benefit to minority groups, then it is also more likely to be considered important to provide meaningful access to the clinical research program by LEP participants. If the need for linguistically appropriate access to the clinical research program in question can rightly be considered "urgent," then the more likely it is that the third factor will weigh in favor of a proactive LEP access program. Since this is determined on a case-by-case basis, it is feasible that certain clinical trials in an institution will require extensive language assistance for LEP participants while it might suffice for other trials to merely offer a foreign language consent form or even less.⁶⁵

In addition to helping determine the nature of the language assistance, the "urgency" question also determines whether a delay in meaningful access or language assistance will be deemed acceptable in a certain clinical trial. For example, according to the OCR guidance, services such as research that are important (either generally to medical knowledge or specifically to the minority groups in question, say, an observational, epidemiological research project about high blood pressure in Latinos) will undoubtedly necessitate a foreign language consent form translated by an expert, but may acceptably permit for interpretation services to be delayed for a reasonable period of time. If, on the other hand, it is both important *and* urgent (say, if a delay in communication may potentially have an adverse impact on the participant's health), then the more likely the particular trial will need both well-translated informed consent documents and supporting literature, as well as real-time interpretation services that are available with little or no delay. Conversely, if the research is seen as relatively "unimportant" and access to linguistically appropriate materials and interpretation is deemed to be non-urgent, then the less likely the OCR will find that the civil right to meaningful access by LEP participants has been violated if little meaningful access is granted LEP participants.⁶⁶

The fourth factor that must be addressed when doing the needs assessment is the resources available

and costs.⁶⁷ Of course, it would be unjust and untenable to demand that 80 percent of an institution's budget go towards recruiting and accommodating a minority population that might comprise 10 percent of the institution's catchment demographic, but it would be similarly unreasonable to expect that we could pro-

for meaningful access given in this article are compelling, there should be a change in the perception of these expenditures as merely "add ons" or "unfunded mandates" and instead be seen as the foregone cost of conducting clinical trials scientifically, legally, and ethically in the United States. Such has historically

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vide "meaningful access" to a previously excluded population with no disproportionate increase in resource spending. At least initially, it will be disproportionately costly to provide "meaningful access" when compared to the community size we want to include. This factor calls for some reasonable mean that will take both of these observations into consideration. Also, any costs associated with linguistically appropriate clinical trial access including translation and interpretation services should be included in the budgetary justifications of proposed clinical trial protocols.

Resource allocation is an important threshold issue in addressing the inequality of access to clinical research by those with LEP. As stated above, the various laws, regulations, and guidelines relating to LEP access remain "unfunded mandates" that in turn, at least in some cases, explicitly state that cost cannot be used as an excuse for inaction.⁶⁸ This may, however, unfairly gloss over the myriad ways in which the current clinical trial enterprise will have to change in order for meaningful linguistic access to be guaranteed to those who need it. Many of the barriers to adequate funding for linguistic competence are institutional and systemic, thus beyond the wherewithal of most individual researchers to fully circumvent. For example, when such expenditures as are necessary to confront this problem are not included in the initial budgets from either researchers or funders (as is currently commonly the case), funds will either have to be shifted from other areas to provide for linguistically-appropriate access, or additional funds will have to be sought from the funder or from novel sources. Neither of these options sounds attractive, although, given the force of the mandate, they remain persuasive. However, if the scientific, legal and ethical justifications

been the case for the sizable costs associated with the scientific, legal, and ethical review of all biomedical research in the United States beginning in the latter half of the 20th century — an era in which clinical research has flourished despite unprecedented regulation and oversight.

The oft-heard excuse of the enormous cost of conducting human subjects research in the United States is not compelling in light of the force of the justifications listed herein and the outsized profits that are the norm for much of research. The problem is not finding the revenue to lift these barriers; rather, it is the much more vexing problem of the equitable reallocation of the plentiful resources already committed to clinical research. And while the political realities concerned are beyond the scope of the present paper, there is policy research being conducted that is finding elegant and practicable solutions to this problem.⁶⁹

The second key element of the safe harbor provision is the development of a written policy on language assistance that is then submitted to the OCR.⁷⁰ The guidance gives models of a good language assistance program that include methods for providing oral and written language assistance.⁷¹

The third key element for a safe harbor is personnel training.⁷² The Guidance stresses that it is necessary not only to have written policies about LEP, but that it is essential for personnel to implement the policies and exhibit the fruits of their training in practice. For many institutions, this will mean cultivating in their research professionals the comfort and ability to work with interpreters in clinical contexts.⁷³ Thus, institutions should strive to maintain a clinical research enterprise composed of linguistically and culturally competent professionals. Studies show that

having professionals trained in cultural and linguistic competency improves research participant satisfaction, understanding, and adherence to protocol.⁷⁴ Having racially, linguistically, and culturally consonant professionals also correlates with better patient satisfaction, understanding, and health outcomes in clinical settings.⁷⁵ If institutions do not have linguistically- and culturally-competent research professionals that can ensure meaningful access for the catchment area's most prevalent language groups, then these institutions should contract with local, medically certified translators, interpreters, and cultural brokers to be reasonably available at short notice to LEP participants.

The fourth and final element in the safe harbor provision is "vigilant monitoring" which requires at least yearly monitoring of the three preceding elements as well as a compilation of feedback from participants and their agents.⁷⁶

The safe harbor provision notwithstanding, an institution may simply choose to implement a comprehensive policy whereby all clinical research materials and communications are linguistically appropriate for the LEP community it serves or should serve. In fact, there are notable academic research institutions that have such a policy in place.⁷⁷ Anecdotal evidence so far suggests that having such comprehensive poli-

California, New York, and Massachusetts are among the states that have comprehensive language access laws. State civil rights laws may also cover this situation when they proscribe direct or indirect discrimination based on ethnicity by all institutions that receive state funding. California's civil rights statutes are an example of this.⁷⁸

Accrediting Agency Requirements

Accrediting agencies can also play an important role in today's governmental climate where much of the standard-setting and policing falls to private organizations such as the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO). This organization requires that hospitals and other health care institutions provide information and communication that is understandable by each patient.⁷⁹ Failure to comply with the accreditation requirements of JCAHO can have serious repercussions for institutions, including loss of accreditation and monetary penalties.

The Ethical Imperative

The Belmont Report, the seminal document that helped usher in the highly regulated environment in which clinical research now operates in the U.S., is well known for its language protecting against the inappropriate inclusion of vulnerable populations in medical research. What is less widely known and seldom written about is that the high regard in which the Belmont Report holds the principle of justice also condemns the inappropriate *exclusion* of those who may wish to participate.⁸⁰ One of the three basic ethical principles upon which this momentous document was founded, justice, for the framers of the Belmont report, is the principle that "equals ought to be treated equally."⁸¹ The report states that

"[a]n injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly."⁸² If it is right to think, as the various laws, cases, guidelines, and regulations surrounding this issue make abundantly clear, that a person is entitled to meaningful access to health services regardless of his or her proficiency in speaking English, then an injustice is apparent in the thousands of clinical trials that fail to accommodate this large and growing segment of the American population. According to the Belmont Report, this apparent discrimination is a violation of its principle of justice if no good reason or evidence of undue bur-

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cies is an excellent way to ensure against possible violations of the statutes and guidelines regarding LEP, to help foster relationships of trust and goodwill with their communities as part of ongoing commitments by these centers, and to serve as an excellent outreach tool for appropriate inclusion of underrepresented groups into clinical trials (which also guards against violating another spate of federal laws and guidelines, most notably the NIH Revitalization Act of 1993.)

State Laws

Some states have also implemented laws and regulations that require health care facilities to provide linguistically appropriate services to LEP patients.

den is offered as a defense by the researchers who wish to discriminate on the basis of language proficiency.⁸³

Conclusion

This paper has argued that limited English proficiency (LEP) is a serious and increasingly common barrier to participation in clinical trials and to the safety of enrolled LEP participants. This is true despite the many clear laws, regulations, and guidelines that mandate linguistically appropriate health services (clinical trials included) to this protected class of people. I outlined in this paper three distinct imperatives (scientific, legal, and ethical) that necessitate the lifting of these barriers. And while further study is necessary to determine whether these disparities render current research practice scientifically unsound, the legal and ethical justifications outlined herein are sufficient to warrant a more rigorous implementation of the policies mentioned in clinical research sites across the country.

Existing laws, regulations, and agency guidelines are unevenly enforced and largely ignored by many in the clinical research enterprise even though they deliberately address the problem of access for LEP persons. This is due to many factors including the underfunding of agencies tasked with oversight and a general ignorance of these rules by researchers and funders. This general non-compliance state of affairs should provide strong incentive for law and ethics scholars as well as clinical research associates to engage in serious deliberation regarding the appropriate response necessary to rectify the situation. I propose that a reconsideration of the current rules and policies that govern clinical trials in light of what we have learned about LEP participants is in order. Though these appear adequate on their face, the reality of an underfunded and overextended oversight mechanism, coupled with the lackadaisical adherence to the regulations by many of those involved in clinical research, lead this author to believe that the various laws, regulations, and guidelines should be revisited by policymakers and reconceived with the current realities of clinical research in mind. In addition, new initiatives to educate and impress upon the clinical research community, including research sponsors, institutions that host research, investigators, and IRB members, the necessity of providing LEP persons with meaningful access to clinical trials are needed.

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 16. A. Mozes, News Article, "Report Claims Clinical Trials Miss Many Populations," *HealthDay News*, April 1, 2008, available at <<http://healthday.com/Article.asp?AID=614031>> (last visited November 18, 2008).
 17. Intercultural Cancer Council, Cancer Fact Sheets, available at <<http://iccnetwork.org/cancerfacts>> (last visited November 18, 2008).
 18. U.S. Census Bureau, *Profile of General Demographic Characteristics: 2000*, at Table DP-1, available at <<http://censtats.census.gov/data/US/O1000.pdf>> (last visited November 18, 2008).
 19. See N. S. Weiss, T. D. Koepsell, and B. M. Psaty, "Generalizability of the Results of Randomized Trials," *Archives of Internal Medicine* 168, no. 2 (2008): 133-135; S. S. Dhruva and R. F. Redberg, "Variations Between Clinical Trial Participants and Medicare Beneficiaries in Evidence Used for Medicare National Coverage Decisions," *Archives of Internal Medicine* 168, no. 2 (2008): 136-140.
 20. Though the scientific imperative is lessened in particular cases of exclusion of LEP participants who are white or whose genetic pharmacogenomic profiles are already adequately represented among trial participants, I contend that there remains a scientific necessity to include LEP persons generally, even though it may not be true severally.
 21. C. N. Rotimi, "Understanding and Using Human Genetic Variation Knowledge in the Design and Conduct of Biomedical Research," *Eliminating Disparities in Clinical Trials (EDICT) Online Reading Room*, available at <http://www.bcm.edu/edict/PDF/Scientific_Rationale.pdf> (last visited November 18, 2008); N. A. Rosenberg, J. K. Pritchard, J. L. Weber, H. M. Cann, K. K. Kidd, L. A. Zhivotovsky, and M. W. Feldman, "Genetic Structure of Human Populations," *Science* 298, no. 5602 (2002): 2381-2385.
 22. International HapMap Project, available at <<http://hapmap.org/>> (last visited November 18, 2008).
 23. C. Ouyang and T. G. Krontiris, "Identification and Functional Significance of SNPs Underlying Conserved Haplotype Frameworks across Ethnic Populations," *Pharmacogenetics and Genomics* 16, no. 9 (2006): 667-682.
 24. G. S. Ginsburg and J. J. McCarthy, "Personalized Medicine: Revolutionizing Drug Discovery and Patient Care," *Trends in Biotechnology* 19, no. 12 (2001): 491-496.
 25. See *supra* note 23.
 26. M. Beckman, News Article, "The Race for Ancestral Genetics in Clinical Trials," *Journal of the National Cancer Institute* 98, no. 18 (2006): 1270-1271.
 27. R. L. Brennan, *Generalizability Theory* (New York: Springer-Verlag, 2001).
 28. *Id.*
 29. It might be charged that I am being unduly "deterministic" in my contention that LEP participants are likely to correspond with underrepresented ancestral genetic groups. However, I do not mean that LEP participants are somehow genetically different from English-proficient persons from the same (or any other) ethnicity. I am simply making the argument that, in the current clinical research environment, where certain genetic profiles are already underrepresented, any blanket exclusion of LEP persons will undoubtedly exacerbate the problem of generalizability of research results.
 30. See Race, Ethnicity, and Genetics Working Group, Review Article, "The Use of Racial, Ethnic, and Ancestral Categories in Human Genetics Research," *American Journal of Human Genetics* 77, no. 4 (2005): 519-532. Note, however, that I do not argue that simply lifting the language barriers to clinical research will solve the scientific problem of generalizability. There are many other barriers to the participation of certain minorities in clinical trials that will undoubtedly continue to conspire against adequate inclusion and thus generalizability. For an excellent, though non-comprehensive compilation of the myriad barriers to clinical research, see J. G. Ford, M. W. Howerton, S. Bolen, T. L. Gary, G. Y. Lai, J. Tilburt, M. C. Gibbons, C. Baffi, R. F. Wilson, C. J. Feuerstein, P. Tanpitukpongse, N. R. Powe, and E. B. Bass, "Knowledge and Access to Information on Recruitment of Underrepresented Populations to Cancer Clinical Trials," *Evidence Report/Technology Assessment No. 122*, prepared for the Agency for Healthcare Research and Quality (AHRQ), June 2005, available at <<http://www.ahrq.gov/downloads/pub/evidence/pdf/recruitment/recruit.pdf>> (last visited Oct. 9, 2008).
 31. I recognize that the scientific rationale for the inclusion of LEP participants in clinical research is, as of this writing, only a *prima facie* imperative. That is, it is certainly conceivable that allelic frequencies get effectively "washed out" as we move upward along the axis I described of ancestral genetic group → ethnicity → LEP participant, or that any allelic frequency profiles along this axis have no impact on pharmacokinetic profiles (though already there is ample evidence to suggest otherwise), or that any possible pharmacokinetic profiles that may be more prevalent in a particular sub-population are already sufficiently represented in today's relatively homogeneous clinical trial populations. My point here is that while any of these possibilities may invalidate my proposed scientific necessity for the inclusion of LEP participants in clinical trials, there remains a *prima facie* imperative until that time when we can disprove it by any of the aforementioned empirically determined possibilities.
 32. §601 of Title VI of the *Civil Rights Act of 1964*.
 33. 65 *Federal Register* 52762, 52763 (August 30, 2000). "In the course of its enforcement activities, OCR has found that persons who lack proficiency in English frequently are unable to obtain basic knowledge of how to access various benefits and services for which they are eligible, such as the State Children's Health Insurance Program (SCHIP), Medicare, Medicaid or Temporary Assistance to Needy Families (TANF) benefits, clinical research programs, or basic health care and social services."
 34. See generally, S. E. Lederer, *Subjected to Science: Human Experimentation in America before the Second World War* (Baltimore: Johns Hopkins University Press, 1995).
 35. B. A. Brody, *The Ethics of Biomedical Research: An International Perspective* (New York: Oxford University Press, 1998): at 186. See, however, C. Walsh and L. F. Ross, "Are Minority Children Under- or Overrepresented in Pediatric Research?" *Pediatrics* 112, no. 4 (2003): 890-895, which shows that at least in some cases, minority participants continue to be overrepresented in certain clinical trials.
 36. *National Institutes of Health Revitalization Act*, 42 U.S.C. § 289a-2 (1993); Public Law 103-43; 59 *Federal Register* 14508 (as republished March 28, 1994), available at <<http://vlex.com/vid/19246381>> (last visited November 18, 2008).

37. *Id.*
38. Executive Order 13166, 65 *Federal Register*, 50121 (August 16, 2001).
39. Executive Order 13166.
40. *Id.*
41. *Id.*
42. Lamentably, even after several reminder letters from the Assistant Attorney General's office and formal deadline extensions, many federally funded agencies have not complied with the requirement to submit LEP guidance per Executive Order 13166. For updates on agency LEP guidance, see <<http://www.usdoj.gov/crt/cor/13166.htm>> (last visited November 18, 2008).
43. 68 *Federal Register* 47311, 47323 (August 8, 2003). The Office of Civil Rights at the U.S. Department of Health and Human Services make available pamphlets in a variety of languages that outline the obligations that Title VI lay out for federally funded institutions and the mechanisms by which persons who have been discriminated against can file complaints with the Office. See <<http://www.hhs.gov/ocr/generalinfo.html>> (last visited November 18, 2008).
44. 45 C.F.R. §80.3(b)(2). Health care was a principal focus of the 2003 guidance. See S. Rosenbaum, "Reducing Discrimination Affecting Persons with Limited English Proficiency: Federal Civil Rights Guidelines under Title VI of the 1964 Civil Rights Act," *Public Health Reports* 119, no. 1 (2004): 93-96. In 2001, the United States Supreme Court narrowed the scope of the proscription for *de facto* discriminatory practices in *Alexander v. Sandoval*, 532 U.S. 275 (2001). In that case, after the promulgation of the Civil Rights Act of 1964, Alabama amended its constitution to make English the official language of Alabama. Alabama's Department of Public Safety took this to justify a requirement that all driving tests must be administered and taken in English. A bare majority of the U.S. Supreme Court held that even if the Alabama Department of Public Safety's failure to provide driving tests in Spanish amounted to a violation of Title VI of the Civil Rights Act of 1964, no private right of action to enforce the regulation existed. However, subsequent Executive Orders, federal regulations, and the 2003 guidance make clear that the onus to remove language barriers in health care lies squarely with federally funded health care facilities and providers. See Executive Order 13166, 65 *Federal Register*, 50121 (August 16, 2001); 65 *Federal Register* 52762 (August 30, 2002); 68 *Federal Register* 47311, 47312.
45. 68 *Federal Register* 47311-47323 (August 8, 2003). U.S. Department of Health and Human Services, Office for Civil Rights, *Guidance to Federal Financial Assistance Recipients Regarding Title VI Prohibition Against National Origin Discrimination Affecting Limited English Proficient Persons*, 2003, available at <<http://www.hhs.gov/ocr/lep/revisedlep.html>> (last visited November 18, 2008).
46. 68 *Federal Register* 47311.
47. *Id.*
48. *Lau v. Nichols*, 414 U.S. 563 (1974).
49. *Alexander v. Sandoval*, 532 U.S. 275 (2001).
50. See for example, U.S. Commission on Civil Rights, "The Health Care Challenge: Acknowledging Disparity, Confronting Discrimination, and Ensuring Equality — Vol. II, The Role of Federal Civil Rights Enforcement Efforts," September 1999, at Chapter 4; B. D. Smedley, A. Y. Stith, and A. R. Nelson, Institute of Medicine, *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care (Executive Summary)* (Washington, D.C.: National Academy Press, 2003): at 12-13 (which concludes that the DHHS's OCR "has suffered from insufficient resources to investigate complaints of possible violations" and recommends increased funding for this purpose.)
51. See *United States Department of Health & Human Services: FY 2007 Budget in Brief: Office for Civil Rights*, available at <<http://www.hhs.gov/budget/07budget/ocr.html#civilRights>> (last visited November 18, 2008).
52. D. Bustillos, "Surveying the Policy Landscape for Eliminating Disparities in Clinical Trials," *Eliminating Disparities in Clinical Trials (EDICT) Online Reading Room*, available at <http://www.bcm.edu/edict/PDF/Policy_Landscape.pdf> (last visited November 18, 2008).
53. §601 of Title VI of the *Civil Rights Act of 1964*; 68 *Federal Register* 47311.
54. 65 *Federal Register* 52762, 52765.
55. 68 *Federal Register* 47311.
56. *Id.*
57. *Id.*
58. *Id.*
59. *Id.*
60. *Id.*
61. *Id.*, at V.
62. 68 Fed. Reg. 47311, 47313.
63. *Id.*
64. *Id.*
65. *Id.*
66. *Id.*
67. *Id.*
68. *National Institutes of Health Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research*, 59 *Federal Register* 14508 (as republished March 28, 1994); Public Law 103-43 § 492B(d)(2).
69. See *Eliminating Disparities in Clinical Trials (EDICT) policy research*, which is concerned with examining and proposing cost-effective solutions, available at <<http://www.bcm.edu/edict>> (last visited November 18, 2008).
70. 65 *Federal Register* 52762, 52766-67.
71. *Id.*
72. *Id.*
73. S. D. Watson, "Reforming Civil Rights with Systems Reform: Health Care Disparities, Translation Services & Safe Harbors," *Washington and Lee Racial and Ethnic Ancestry Journal* 9, no. 13 (2003): 13-34, at 32.
74. N. L. Oliva, "When Language Intervenes: Improving Care for Patients with Limited English Proficiency," *American Journal of Nursing* 108, no. 3 (2008): 73-75; S. L. Taylor and N. Lurie, "The Role of Culturally-Competent Communication in Reducing Ethnic and Racial Healthcare Disparities," *American Journal of Managed Care* 10, Special Supplement (2004): SP 1-4.
75. S. Saha, M. Komaromy, T. D. Koepsell, and A. B. Bindman, "Patient-Physician Racial Concordance and the Perceived Quality and Use of Health Care," *Archives of Internal Medicine* 159, no. 9 (1999): 997-1004; T. A. Laveist and A. Nuru-Jeter, "Is Doctor-Patient Race Concordance Associated with Greater Satisfaction with Care?" *Journal of Health and Social Behavior* 43, no. 3 (2002): 296-306.
76. 65 *Federal Register* 52762, 52765-66.
77. For example, the Texas Tech University Health Sciences Centers in west Texas have implemented an institution-wide policy to have relevant clinical trial materials translated into Spanish, the area's second most popular language.
78. See California Constitution, art. I, § 31.
79. Joint Commission on the Accreditation of Health Care Organization, "Provision of Care, Treatment, and Services," 2007, at Standard PC.6.10. "The patient receives education and training specific to the patient's needs and as appropriate to the care, treatment, and services provided."
80. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, Department of Health, Education, and Welfare, *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, OPRR Reports, 1979, at Part B, 3, available at <<http://ohsr.od.nih.gov/guidelines/belmont.html>> (last visited November 18, 2008).
81. *Id.*
82. *Id.*
83. *Id.*